

Risks, Benefits, and Conflicts of Interest in Human Research: Ethical Evolution in the Changing World of Science

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A generation ago, we adopted a national system for the protection of human subjects in research. Today, that system is facing new challenges. Many argue that the system has failed to evolve in concert with dramatic changes in the research environment. Accordingly, efforts are underway to reform the existing process to make it both more efficient and more effective. At the same time, many are also reexamining the system in more fundamental ways — going well beyond considerations of policies and compliance and raising questions that go to the very foundations of what constitutes an ethical conduct of human research.

Experimentation involving human subjects is a necessary step in the process of translating scientific discovery and technological advancement into processes and products that offer the prospect of better lives for all of us. It helps us to better understand who we are, the things we do and believe what we believe, and, whether biomedical or social in nature, is an endeavor that is strongly supported by the public and one that offers hope to many. Because society is the ultimate beneficiary of our research endeavors, society also bears responsibility for ensuring that the interests of those who accept the risks of research participation are understood and protected. Most, if not all, research involves risk — social, behavioral, psychological, and economic risks as well as physical risks — which often exceed in magnitude and probability the “minimal risk” we encounter in our daily lives. Accordingly, the ethical framework in which we conduct research requires that we carefully consider the risks and potential benefits associated with research as we decide whether or not to pursue a particular study. These considerations are undertaken within the framework of ethical principles delineated by the National Com-

mission for the Protection of Human Subjects of Biomedical and Behavioral Research in *The Belmont Report*: respect for persons, beneficence, and justice.

Our system for approval and oversight of human research has depended heavily — indeed, almost exclusively — on the exercise of the collective wisdom and judgment of individuals serving on review committees now known as institutional review boards, or IRBs. Our IRBs are charged with making determinations of whether or not research should be done at all, if so, how it should be done so as to protect the interests of the research subjects within the existing ethical framework and in compliance with relevant regulations. Analysis of risks and potential benefits is intended to be a key element of the review process; and while the IRBs approach this task with every good intention, the task is one that cannot be easily changed. Moreover, there are clear signs that the analysis is not likely to get any easier as the research environment grows ever more complicated.

This increasing complexity is the result of several interdependent factors. These include the increasing technical complexity of the research, the questions being asked and the tools being used, the milieu in which the research is being conducted, and the relationships between those who sponsor the research and those who will conduct it and, in turn, their relationships with the actual participants.

We now recognize that questions about risks and benefits for individuals that once seemed to be relatively straightforward are often not so simple. This issue of the *Journal* includes four papers that explore these matters in detail and raise several important questions. In particular, they emphasize the need for us to broaden our perspective when we consider risks and benefits in research by asking a simple question — benefits and risks to whom?

By asking this simple question, we in fact acknowledge the uncertainty and even ambivalence that has taken root

in our consciousness as we examine our research activities. While we may have once approached questions of risk and benefit from an almost detached perspective, we now seem to be — or at least are becoming — more keenly aware that the perspectives of all parties to the research must be considered. We further appreciate that these perspectives signify different interests that are not easily segregated, and they are often in conflict. Not surprisingly, decision-making is considerably more complicated when multiple interests are interwoven into the fabric of research, and our moral calculus may not yet be sufficiently well developed to approach these complex situations with facility.

Connectedness is increasingly recognized as an important principle within the ethical framework for responsible human research. Stemming directly from so-called “feminist” philosophical principles, the notion of *connectedness* is that decision-making and personal actions must take into consideration not only the decision-maker, but also other persons and events associated with the decision-maker. While making decisions in a detached manner may foster great objectivity and impartiality — the hallmarks of principle-based decision-making — it can also lead to decisions and actions that ignore the broader impact of those actions and decisions on loved ones, family, community, and even society at large.

As we undertake new research initiatives, such as genetic manipulation and international research that brings into immediate juxtaposition divergent cultural norms and socioeconomic disparities, sensitivity to the impact of our research and to our moral obligations to those who make the research possible requires thoughtful consideration of the broader context of neighbor, community, and society. Similarly, as we understandably increase the extent to which needed research is conducted on vulnerable populations, such as children, it may well be necessary to redefine our

notions of consent and assent for purposes of recruiting subjects.

Today, IRBs are being called upon to exercise their judgment and authority in this enriched context, often without the benefit of extensive public discourse. The moral dilemmas they encounter are frequently without solid precedent or consensus to offer guidance. The decisions reached under such conditions are often controversial and are greeted with cries of unethical behavior. Such claims certainly reflect that the activity in question may be objectionable to some, but calling it unethical does not in itself make it so. Still, the apparent increase in the frequency of human research activities that are considered by some to be unethical — and our increasing awareness of the financial and personal arrangements that raise questions of impropriety and conflicts of interest — give us reason to pause and take a closer look at how we decide what research *should* be done and how we should evaluate and balance the interests of the many parties involved in the research.

Dr. Michael Grodin, a friend, teacher, and colleague for many years, once said that “ethical dilemmas are hard because they are hard ... there are no easy ethical dilemmas.” One approach toward their meaningful resolution is to broaden the discussion and acquire more information. Given the current scale and pace of change we are now witnessing in the domain of human research, one can hardly imagine a more appropriate course of action or a more appropriate time to follow it. And as we engage in this discourse, let us do so with reason and passion, as well as a sincere sense of compassion, for all of them enrich and inform the debate. Doing so will ensure that the conclusions we reach and the future directions we take will reflect both the noble goals of science to which we look for hope, and those values that guide us to actions of which we can be justly proud.